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Dose-Response Correlation of Methadone and its Metabolite EDDP in Human Hair

Sixth Technical Report

(Time period covered: January 1 - March 31, 1996)

Start of the Third Series and Analysis of the Samples of the Second Test Series

We were able to arrange for the patients of two further Methadon practices, that of Dr. Sachtleben in Pirmasens and Dr. Lueg in Kaiserslautern, to take part in our study. They were treated in the same manner as described in our previous Technical Reports. In this new series, the applied sweat patches were generally well accepted. Up until now only one patient (L2) has complained about irritations from the last patch. Blood was drawn by the personnel of the two practices. Hair strands were cut and bleached in the same manner as described previously. One patient from Kaiserslautern agreed only to give sweat and blood samples, another quit the program after collection of sweat patches and bleaching and cutting of the first hair strand. Nevertheless, this subject could be convinced to give blood and a small hair sample from the bleached strand to evaluate her individual hair growth window.

The sweat patches from Saarbruecken, Kaiserslautern and Pirmasens were analysed according to the method developed in our laboratory (see Technical Report 3). A first evaluation of these results seems to confirm our previous findings (see also Technical Report 3). No lag time could be observed under chronical treatment. In addition

to our first analysis, we could prove besides heroin and/or cocaine consumption the consumption of codein and/or DHC. We have attached the results of the sweat patch analysis in 5 tables at the end of this report. One table represents the data collected in one practice. On the left and right side, one can find the number of the subject and the substances analyzed. At the top, the days of removal are listed (day of application = day 0).

In addition to the sweat patch analysis, we began preparing the hair and blood samples for analysis.

After further studies and a re-evaluation of our previous findings on the individual hair growth, we came to the conclusion, that the so-called average hair growth-range (see Technical Report 1) is not a useful tool for a reliable examination of sectional hair analysis since it does not give an adequate description of hair growth. Too many individual factors like hereditary factors, nutrition, hormonal factors, age, diseases or medication, may influence the hair growth of a subject. The use of a class distribution instead of a mean value of hair growth rate seems to be a more appropriate method for handling the problem in segmental hair analysis. Our studies showed that a class ranging from 7.5 to 13.5 mm/28 days matched the correct time window in most of the cases. Nevertheless, this still is just a coarse approximation. Whenever discrepancies between the results of hair analysis and the history on record appear, or a subject claims pathological or very fast or slow hair growth, a determination of the individual hair growth is indicated. This may be done by our bleaching method. Additionally, we observed that the anagen hair follicles are embedded at least 1-4 mm, sometimes even 6 mm, within the scalp. Therefore a delay due to intradermal hair growth which ranges between 1-4 weeks should be kept in mind when the results of a sectional analysis are interpretated.

We also started to study the efficiency of different extraction methods for opiates and compared:

a. extraction method according to Baumgartner,

b. extraction method according to Moeller,
c. extraction with acidic methanol according to Pragst or Kauert,
d. extraction with acetone and methanol,
e. extraction with 4-methylpentan-2-on

Our findings suggest that:

- Powdered hair is a better extraction matrix than intact hair strands.
- Buffers and water molecules containing organic solvents (W) are better for codeine extraction than no water molecules containing solvents (NW). Non-swelling solvents like 4-methylpentan-2-on showed a significant decrease. The extraction gave only about 5-10 % of the yield obtained by aqueous extractions.

The study was done on codein-containing hair. Further preliminary studies indicate that the extractibility of drug substances from the hair matrix may well be influenced by the physico-chemical properties of the particular drug substance, its stability under the extraction conditions as well as by the penetration of the extraction solvent into the hair matrix. These influences are going to be studied further on hair fibres from methadone-treated patients. Additionally, in vitro experiments on melanin affinity of methadone will be performed within the next weeks.